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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/337,746	06/22/1999	GREGORY M. GLENN	PM-254811	9348

7590 09/27/2004

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/337,746	GLENN ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71,72,74-87 and 89-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71-72, 74-87, 89-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendments and remarks filed 7/15/04 have been entered.

2. New Claims 71-72, 74-87, 89-95, and newly added Claims 96-97, are pending and under examination.

3. In view of Applicant's amendment and remarks only the following rejections remain.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 71-72, 75-87, and 90-95, and newly added Claims 96-97, stand/are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for,

a method for transcutaneous immunization (TCI) comprising applying a formulation to hydrated skin,

does not reasonably provide enablement for,

a method for dry TCI, i.e., a method wherein no hydration of the skin has been performed and wherein a dry formulation is employed.

Applicant's arguments, filed 7/15/04, have been fully considered but they are not persuasive. Applicant argues that the specification enables a method in which hydration is not a critical limitation at numerous cites.

As set forth previously, the success of the instant method must be considered unexpected and thus highly unpredictable. Accordingly, mere assertions that the method works, e.g., the cites at pages 35 and 40 of the specification, cannot be considered to be enabling. The specification does, however, comprise 62 examples; in 60 of these examples the skin is either prehydrated or the "dry" formulation is dissolved in solution and

placed on the skin (effectively hydrating the skin at the time of TCI).

In Example 61 a dry formulation is placed on the non-hydrated skin of 5 experimental animals. A review of the results shows that said results vary substantially from essentially background (titer=53) to minimal (titer=1750). These scientifically insignificant results seem to at best indicate the method of a dry formulation on non-hydrated skin is unpredictable. Also note that the final step of the experiment was to wash the dry formulation off the skin of the animal. It is likely that this washing step effectively comprised a certain degree of uncontrolled hydration which could explain the inconsistent results.

The results of Example 62 would seem to be more straightforward. In 3 of 5 experimental animals (i.e., a majority of experimental animals) the post TCI titer in animals wherein a dry formulation was placed on the non-hydrated skin was *below background*. The other 2 animals showed only at best a minimal response. Accordingly, it remains the Examiner's position that the method encompassed by the instant claims wherein no hydration of the skin has been performed and wherein a dry formulation is employed must be considered to be highly unpredictable and requiring of undue experimentation.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321c may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. As set forth previously, Claims 71-72, 74-87, 89-95, and newly added Claims 96-97 stand/are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 3-35, 50-77, and 79-111 of copending Application No. 09/266,803. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the instant application recite a method of TCI comprising employing an ADP-ribosylating exotoxin to induce an immune response. The claims of the '803 application recite a method of inducing an immune response employing a generic ADP-ribosylating exotoxin (Claim 30-33) or specific ADP-ribosylating exotoxins (Claims 22-26). The methods are therefore not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. As set forth previously, Claims 71-72, 74-87, 89-95, and newly added Claims 96-97 stand/are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 2, 5, 6, 11, 19, and 32 of copending Application No. 10/633,626. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims encompass a method comprising inducing an immune response (TCI) comprising applying a formulation comprising an adjuvant or an antigen and an adjuvant.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. As set forth previously, Claims 71-72, 74-87, 89-95, and newly added Claims 96-97 stand/are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 2, 5, 6, 11, 19, and 32 of copending Application No. 10/701,069. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims encompass a method comprising inducing an immune response (TCI) comprising applying a formulation comprising an adjuvant or an antigen and an adjuvant.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. As set forth previously, Claims 71-72, 74-87, 89-95, and newly added Claims 96-97 stand/are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1, 5, 12, 14, and 17 of copending Application No. 10/435,676. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims encompass a method comprising inducing an immune response (TCI) comprising applying a formulation comprising an adjuvant or an antigen and an adjuvant.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant indicates that a terminal disclaimer over the '803 application will be filed upon the indication of allowable subject matter. Applicant has not addressed the additional double patenting rejections.

Applicant is advised that failure to address the additional double patenting rejections in response to this action will be held non-responsive.

11. Claims 71-72, 74-87, 89-95, and newly added Claims 96-97 stand/are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, the specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) a "a modified ADP-ribosylating exotoxin ... modified to be less toxic" (Claims 71 and 81),

C) "a formulation comprised of antigen and adjuvant" (Claim 81),

D) "[heat] killed rabies virus" (Claim 85).

Applicant's arguments, filed 7/15/04, have been fully considered but they are not persuasive. Applicant argues that, Regarding A), support is provided in original Claim 53 and the specification provides support at page 34.

Regarding A), original Claim 53 is not of equivalent scope as the instant claims. First, the original claim recites "genetically or chemically modified" and not the broader "modified" as is now claimed. Second, the original claim does not comprise the new limitation of Claim 71 that the formulation "does not contain molecules having only antigenic activity". At page 34 the specification discloses only "genetically altered toxoids" and not the modified exotoxins of the instant claims.

Applicant argues that, Regarding C), support is provided in original Claim 53 and throughout the specification. Applicant again cites the specific Examples of the specification

As set forth previously, original Claim 1, specifically excluded a formulation comprising a separate antigen and adjuvant (as now claimed). Applicant appears to be trying to cite fragments of the claim to improperly cobble together a new claim of different scope. Also, as set forth previously, regarding the examples, examples disclosing specific formulations administered to specific mouse strains cannot be considered sufficient written description to support generic methods. i.e., the examples disclosing the administration of specific formulations (e.g., CT and BSA) to BALB/c mice cannot support claims drawn to the generic administration of any formulation to any subject. Applicant argues that the multiple examples provide support for the full scope of the claims. It is noted however, that while the Examples employ antigens and adjuvants that might be considered representative of the full scope of the formulations used in the method of the claims, the Examples do not provide adequate support for the full scope of the complete method of the claims wherein the claims would encompass the use of the formulations of the claims in a method of TCI performed on any organism. The only organism of the methods is a BALB/c mouse which cannot be considered representative of all organisms.

Applicant argues that, Regarding D), removal of the word "heat" renders the rejection moot and Claim 85 does not contain a genus.

Regarding D), again, a specific example cannot support a generic claim. The killed rabies virus is only disclosed in a single example wherein BALB/c mice are immunized by a specific protocol. The claim, however, is indeed generic in that it recites a method wherein any organism is immunized with killed rabies virus by any encompassed TCI protocol. Accordingly, the disclosure in the specification is not commensurate in scope with the method as now claimed and, thus, provides insufficient

written description for the instant method.

Applicant argues that the Office (i.e., the Examiner of record) seems to have confused the enablement requirement with the written description requirement.

Applicant is advised that the instant rejections of Section 11 are for a lack of adequate written description and not for lack of enablement. While the word "scope" might be use in both contexts, the rejections are separate and distinct, i.e., a "scope of enablement" rejection is not a rejection for inadequate written description wherein the disclosure of the specification is not commensurate in "scope" with the invention of the claims.

12. The following are new grounds for rejection.

13. Claims 71 and 81 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 104 of U.S. Patent No. 6,797,276. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims encompass a method comprising inducing an immune response (TCI) comprising applying a formulation comprising an ADP-ribosylating exotoxin (*E. Coli* heat-labile enterotoxin).

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 72 and 87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically, "entertoxin" is properly "enterotoxin".

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

18. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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9/23/04

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